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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/830,033 | 10/22/2001 | Patrick C. Kung | YALE-025/02US<br>306577-2036 | 9303 |

58249 7590 12/30/2008

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| EXAMINER | |
|---|---|
| BORIN, MICHAEL L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1631 | |

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| 12/30/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/830,033 | KUNG ET AL. | |
| | Examiner | Art Unit | |
| | Michael Borin | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *83,84,87 and 88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *83,84,87,88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/18/2008 has been entered.

## Status of Claims

Claims 83,84,87,88 are pending. There are no amendments to the claims.

## *Claim Rejections - 35 USC § 103*

Claims 83,84,87,88 are rejected under 35 U.S.C. 103(a) as obvious over Khwaja et al (US Patent 6113907) in view of Lochardt (US patent 6040138) or Xiong et al. (Molecular Breeding 4: 129–136, 1998) and Wallace et al (Molecular Medicine Today. Volume 3, Issue 9, September 1997, pages 384-389), and further in view of Ray et al. (US 4,570,380)

The claims are directed to method for method for assessing the equivalency of a test batch of an herbal composition to a standardized batch by using genomic-based assay and comprising the steps of comparing gene expression detected by hybridizing test and standardized herbal compositions, comparing the gene expression, and assessing equivalency of expression in the test and standardized batches for the purposes of quality control.

Khwaja et al discloses a method for manufacturing pharmaceutical compositions from plant extracts wherein quality control is perform via standardization and control to provide reproducible material in the predictable and consistent treatment of patients (column 2, lines 39-51).

The method of Khwaja et al. comprises harvesting botanical material (whole or part), determining standardized bioactivity profile, comparing the calculated bioactivity of the botanical composition to a bioactivity fingerprint standard, and determine whether the botanical material is a pharmaceutical grate St. John's Wort (column 9, line 50 to column 2, line 7). The reference does not teach use of genomic based bioassays but teaches that use of bioassays is necessary for ensuring quality of a botanical product.

Complex plant materials and extracts exist which have potent, but relatively unpredictable, medicinal properties. These materials are, for the most part, useless in a clinical setting because of the inherent risks involved with treating patients with poorly characterized materials which have no established batch consistency and which may differ widely in composition. Accordingly, there is a need to provide methods for standardizing such complex botanical materials

The use of gene arrays for content control is well known in the art. See, for example Lochardt (US patent 6040138) describing use of gene arrays for monitoring the expression levels of a multiplicity of pre-selected genes in the presence of large abundance of non-target nucleic acids. See abstract and col. 2. The gene array method of Lochardt is useful in particular for identification of differential gene expression between two samples. See col. 10, line 23. Alternatively see Xiong et al. teaching differential gene expression profile of the whole batch of plant extract via a genomic-based bioassay. See Abstract.

Also see review of Wallace et al emphasizing that DNA chips is a major advance in testing complex mixtures which provide much faster and more reliable assay. See Abstract and throughout the reference.

Further, one skilled in the botanical art at the time the invention was made was fully aware of gene expression in plants, importance of understanding of gene expression for quality control - See Ray et al, (Abstract (last two lines) and claims 1-22, for example) – as well of use of differential gene expression profiles of the whole batch of plant extract via a genomic-based bioassay - see Xiong et al.

In *KSR Int 'l v. Teleflex*, the Supreme Court, in rejecting the rigid application of the teaching, suggestion, and motivation test by the Federal Circuit, indicated that

> The principles underlying [earlier] cases are instructive when the question is whether a patent claiming the combination of elements of prior art is obvious. When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.

*KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007).

Applying the KSR standard of obviousness to the references discussed above, Examiner concludes that using the known technique of gene array analysis of gene expression instead of bioassay in the method of Khwaja et al would have been obvious to one of ordinary skill. The nature of the problem to be solved – comparison between herbal compositions for the purpose of quality control may

lead inventors to look at references relating to new and improved methods of assaying the content of herbal compositions. Therefore, it would have been obvious to use the more advanced method of gene expression analysis described, for example in Lochardt , Xiong or Wallace. As one skilled in the bootanical art was aware of importance of understanding of gene expression for quality control, using the known technique gene expression analysis to provide the desired information for the quality control would have been obvious to one of ordinary skill.

In addition it will be *prima facie* obvious to one skilled in the art at the time the invention was made to be motivated to use genomic-based assays, such as described in Lochardt or Xiong or Ray or Wallace, for example, in the method of Khwaja et al to provide control of the content of herbal preparations samples in the method of Khwaja. One of ordinary skill in the art would not be confined by the particular assays taught in the method of Khwaja and will have reasonable expectation of success that genomic-based assays will be equally effective.

Response to arguments

Applicant's concerns are addressed in the revised rejection above. In particular, Applicant differentiates instant method as using whole extracts. If applicant means that the instant composition is multi-component compared to "individual fractions" of Khwaja, then the Khwaja method is not limited to "individual fractions' but addresses testing of full extract as well –see col. 13, lines 59-61. In addition, the individual fractions of Khwaja are not single

components, but may comprise a plurality of compounds (see col. 10, lines 7-8), which also reads on the “composition comprising multiple chemical components derived from one or more whole plants or plant parts" as instantly claimed. See further reference of Xiong teaching of differential gene expression profiles of the whole batch of plant extract via a genomic-based bioassay.

As for the argument that Teodorescy Declaration asserts that “it is not customary for someone working in botanical products to be familiar with and/or scan the gene expression”, Examiner respectfully disagrees and directs applicant’s attention to the exemplary references of Xiong and Ray used now in rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Marjorie Moran can be reached on (571)272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Borin/
Primary Examiner, Art Unit 1631

mlb